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Multiple evanescent white dot syndrome following COVID-19 vaccines

Multiple evanescent white dot syndrome (MEWDS) usually affects myopic but otherwise healthy young women.[1] Patients present with blurry vision, photopsia, dyschromatopsia, and paracentral and temporal scotomas.[1] This disease is characterized by unilateral grey–white lesions in the outer retina or retinal pigment epithelium with associated foveal granularity.[1]

A case of MEWDS-like retinopathy was described previously following COVID-19 infection.[2] Similarly, COVID-19 vaccines, designed to produce an immune reaction toward the target COVID-19 protein, presumably could contribute to triggering the processes responsible for MEWDS. The purpose of this correspondence is to report cases of MEWDS following COVID-19 vaccine administration.

This retrospective small case series reports results from the COVID-19 Eye Registry, a Canadian national registry recording ocular manifestation following COVID-19 infections or vaccine administration. Patients with MEWDS reported between December 2020 and September 2021 are included. Basic demographic data, type of vaccine (i.e., Moderna Spikevax [ModernaTX, Inc, Cambridge, Mass.], Pfizer-BioNTech Comirnaty [BioNTech Manufacturing GmbH, Mainz, Germany], or AstraZeneca Vaxzevria [AstraZeneca Canada Inc, Mississauga, Ont.], and Verity/SII and Covishield [Verity Pharmaceuticals Inc., Ewing, New Jersey and Serum Institute of India, Pune, India]), timing of presentation relative to the vaccine, clinical presentation, and final visual acuity (VA) were reported.

Case 1 is a 28-year-old female known for oral herpes simplex virus who presented 2 weeks following her second dose of Moderna vaccine with flashes and decreased VA in her right eye. Initial VA was 20/60, and the anterior segment was unremarkable with no anterior or vitreous cells. Posterior-segment examination revealed multiple small deep grey–white lesions throughout the posterior pole. Fluorescein angiography (FA) showed early hyperfluorescent lesions in early frames with late staining of these lesions in a wreathlike configuration (**Fig. 1**). Fundus autofluorescence (FAF) showed widespread punctiform hyperautofluorescent foci corresponding to the lesions on examination (**Fig. 2**). Macular optical coherence tomography (OCT) showed disruption of the outer retina with hyperreflective projections extending to the outer nuclear layer. The left eye was normal. The initial uveitis investigation panel was negative, including chest x-ray and QuantiFERON-TB Gold (QIAGEN, Hilden, Germany) and (T. pallidum enzyme immunoassay). One month following the vaccine, VA improved spontaneously to 20/25. FAF showed significant regression of the lesions without treatment, and macular OCT normalized.

Case 2 is a 27-year-old male with no known past medical history who presented 22 days following his first dose of Pfizer-BioNTech vaccine with a 1-week history of flashes in the right eye. Initial VA was 20/20, there was no inflammation in the anterior segment or vitreous, but there was blunting of the foveal reflex and multiple deep greyish posterior-pole lesions. FAF, FA, and macular OCT were suggestive of MEWDS. The left eye was normal. The initial uveitis investigations were negative, including chest x-ray and QuantiFERON-TB Gold, angiotensin-converting enzyme, serum lysozyme, and treponemal testing (*Treponema pallidum* enzyme immunoassay). Six weeks following the patient's first dose, the number of lesions decreased significantly, and 3 months postvaccine, all the lesions had resolved without treatment. The patient was examined 2 weeks after his second dose, and no new lesions were observed and VA remained at 20/20.

Case 3 is a 26-year-old healthy female who presented 5 days following her second dose of Pfizer-BioNTech vaccine with a subjective increased blind spot and photopsia in the left eye. Examination revealed 20/20 VA, no relative afferent pupillary defect, normal colour vision using the Hardy–Rand–Rittler pseudoisochromatic test, and an unremarkable anterior segment with no anterior-chamber or vitreous inflammation. Posterior examination revealed pigmentary punctiform changes in the posterior pole. The optic nerve heads were normal without edema. Humphrey automated 24-2 and 10-2 visual fields were normal without increased blind spots. FA revealed early hyperfluorescent lesions in the early frames with late staining of lesions. Macular OCT were normal. The initial uveitis investigations were negative, including chest x-ray and QuantiFERON-TB Gold, angiotensin-converting enzyme, serum lysozyme, and treponemal testing (*T. pallidum* enzyme immunoassay). A computed tomography scan of the head and orbits also was normal. Four months following the vaccine, VA remained 20/20, all the lesions had disappeared, and FA normalized without intervention.

MEWDS is relatively rare.[1] Although the etiology is unknown, possible autoimmune or autoinflammatory causes have been hypothesized.[1] Our patients presented with typical symptoms of MEWDS, which include decreased VA, photopsia, central scotoma, and increased blind spots.[1] Multimodal imaging is essential in diagnosis and follow-up. Classic presentation on FA includes hyperfluorescent lesions in early phases with a wreathlike configuration. FAF is another noninvasive tool that allows us to follow the hyperautofluorescent lesions in time. Finally, macular OCT shows hyperreflective lesions extending from the retinal pigment epithelium into the ellipsoid zone and outer nuclear layer.[1] Although not seen in case 3, patients can have increased blind spots on visual field testing.[1] No treatment is usually required because most lesions disappear without visual sequelae.[1]

MEWDS following different types of vaccines is well described in the literature, with more than 9 reports including different types of vaccines.[3] A case of recurrent

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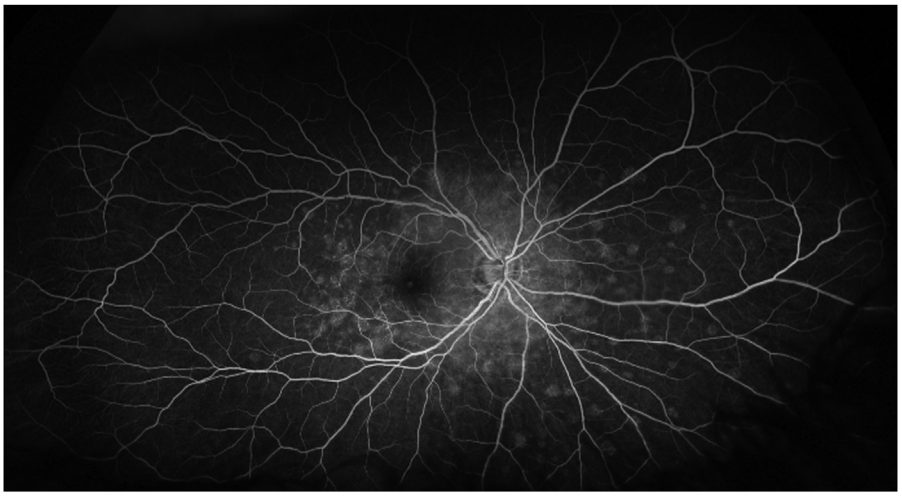

Fig. 1—Fluorescein angiography performed in case 1 showing hyperfluorescent lesions with late staining in a wreathlike configuration.

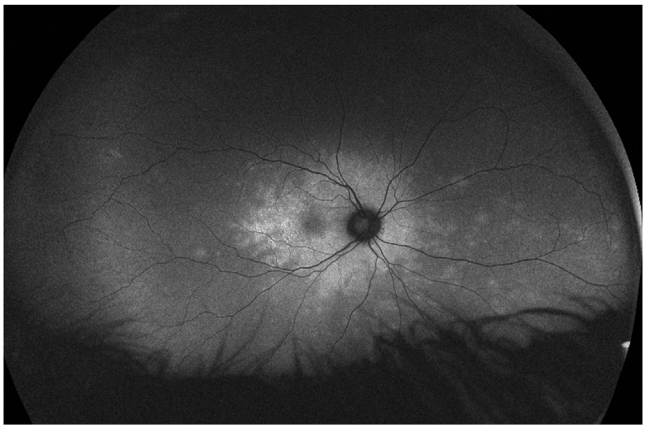

Fig. 2—Fundus autofluorescence showing widespread punctiform hyperautofluorescent lesions distributed in a wreathlike configuration around the macula and optic nerve.

MEWDS in a patient who had previously had an episode of MEWDS was recently reported after COVID-19 vaccination.[4] This contrasts with the 3 cases described herein, in which the patients were newly diagnosed with MEWDS.

Inflammatory ocular and systemic complications following COVID-19 vaccination have been reported and summarized previously.[5] These include anterior uveitis, bilateral panuveitis, bilateral multifocal choroiditis, and reactivation of Vogt—Koyanagi—Harada disease.[5] Other retinopathies following COVID-19 vaccines have been described, including acute macular neuroretinopathy.[5] In an efficacy study on COVID-19 RNA vaccine, spike-specific T cells and binding antibodies were detectable in the serum as early as 10 days after the first dose of the vaccine.[6] Moreover, it has been shown that T cells play a significant role in autoimmune diseases, including uveitis.[7] Consequently, elaboration of an early and robust T-cell response presumably plays a role in patients who develop coincident immune reactions following vaccination. Likewise, the timeline of that early response could support the temporality of our patients' symptoms.

Furthermore, ocular complications following COVID-19 infection also have been reported, including bilateral anterior uveitis and retinopathies.[5] It is crucial to understand that these complications are relatively rare given the mass vaccination campaign with billions of doses administered worldwide and could be coincidental. No scientific evidence suggests that patients should not get vaccinated for ocular complications.[5]

It is impossible to ascertain the causal relationship between COVID-19 vaccines and the described presentations. Given the number of vaccine doses administered, it is likely for rare events to occur after vaccination, even coincidentally. However, the temporal relationship is suggestive of an association in the absence of an alternative explanation.

In conclusion, following COVID-19 infection or vaccination, patients may be at risk for developing new-onset MEWDS. Physicians should be aware of this to elicit the diagnosis in these situations and counsel and follow patients appropriately. There is still no evidence suggesting ocular complications are a contraindication for vaccination given that MEWDS is a self-resolving condition that rarely causes visual sequelae.

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Footnotes and Disclosure

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